PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Blake Dawson Waldron
Level 39
101 Collins Street,
Melbourne
VIC 3000,
Australia

BLAKE DAWSON WALDRON
PATENT SERVICES
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PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *day/month/year* 28 JUL 2004

Applicant's or agent's file reference
WJP:SJ:1337 5913

IMPORTANT NOTIFICATION

International Application No.	International Filing Date	Priority Date
PCT/AU2003/000381	28 March 2003	28 March 2002

Applicant
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translations to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide

Name and mailing address of the IPEA/AU	Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	JENNIFER FERNANCE Telephone No. (02) 6283 2269

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference WJP:SJ:1337 5913	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/AU2003/000381**	International Filing Date *(day/month/year)* 28 March 2003	Priority Date *(day/month/year)* 28 March 2002
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] A61K 38/45, 38/48, A61P 35/00		
Applicant COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANIZATION et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

   [X] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 4 sheet(s).

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [ ] Certain observations on the international application

Date of submission of the demand 4 September 2003	Date of completion of the report 19 July 2004
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **JENNIFER FERNANCE** Telephone No. (02) 6283 2269

INTERNATIONAL PRELI[redacted]RY EXAMINATION REPORT

[redacted]ternational application No.
PCT/AU2003/000381

I. Basis of the report

1. With regard to the **elements** of the international application:*

- [ ] the international application as originally filed.
- [X] the description, pages **1-21** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [X] the claims, pages , as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages **22-25** received on **3 December 2003** with the letter of **3 December 2003**
- [X] the drawings, pages **1/12-12/12** as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examinatio[redacted]..6.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	**1-28**	**YES**
	Claims	-	**NO**
Inventive step (IS)	Claims	**13, 14, 26, 27**	**YES**
	Claims	**1-12, 15-25, 28**	**NO**
Industrial applicability (IA)	Claims	**1-28**	**YES**
	Claims	-	**NO**

2. Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this opinion:

D1: AU-A-27868/00

Novelty (N) Claims 1-28

Claims 1-28 meet the criteria set forth in PCT Article 33(2) for novelty. The prior art published before the priority date does not disclose compositions comprising an engineered ovine atadenovirus and a lipid or their use as presently claimed. Therefore the subject matter of the claims is novel and meets the requirements of Article 33(2) PCT with regard to the requirement for novelty.

Inventive Step (IS) Claims 1-12, 15-25, 28

The problem to be solved is that of the delivery of a GDEPT system in gene therapy. The Applicant has solved this problem by the use of a GDEPT system based on OadV and a cationic lipid.

D1 discloses the presently defined OadV in the treatment of cancers. The admitted prior art at page 10 discloses that, at the time of priority, cationic lipids were known to help facilitate transduction and to enhance viral infectivity. Therefore it is considered that the invention as claimed in claims 1-12, 15-25 and 28 lacks inventive step in light of D1 and the common general knowledge of the art of molecular biology and gene therapy.

Claims 13, 14; 26 and 27 meet the criteria set out in PCT Article 33(3) with regard to the requirement of inventive step because the prior art does not obviously suggest to a person skilled in the art compositions comprising the atadenovirus and the specific lipid or their use as claimed

Industrial Applicability (IA) Claims 1-28

Claims 1-28 are considered to be industrially applicable.

CLAIMS

1. A method of treating a solid tumour in a subject, the method comprising the following steps

(i) delivering to the solid tumour a composition comprising an engineered ovine atadenovirus and a lipid; and

(ii) administering a prodrug to the subject,

wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts the prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.

2. A method as claimed in claim 1 in which the promoter is selectively active in a specific tissue.

3. A method as claimed in claim 1 or claim 2 in which the solid tumour is prostate cancer.

4. A method as claimed in claim 2 or claim 3 in which the specific tissue is prostate tissue.

5. A method as claimed in any one of claims 1 to 4 in which the promoter is a prostate specific membrane antigen promoter.

6. A method as claimed in any one of claims 1 to 5 in which the promoter is a probasin promoter.

7. A method as claimed in any one of claims 1 to 6 in which the ovine atadenovirus further comprises a transcriptional enhancer element.

8. A method as claimed in claim 7 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.

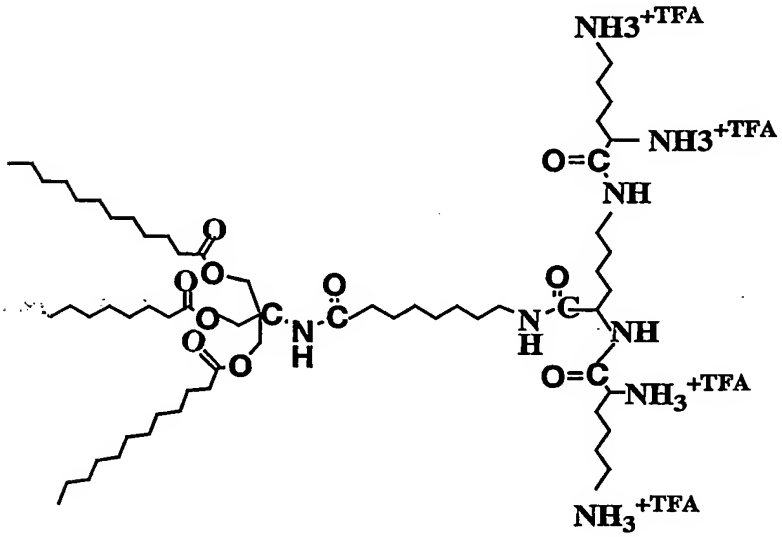
9. A method as claimed in any one of claims 1 to 8 in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase /5-flurocytosine, human cytochrome P450/cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-flurouridine, cytosine kinase/cytosine arabinoside, *E. coli* GPT/ 6-thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyriboside or fludarabine.

10. A method as claimed in any one of claims 1 to 8 in which the enzyme is a purine nucleoside phosphorylase (PNP)and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.

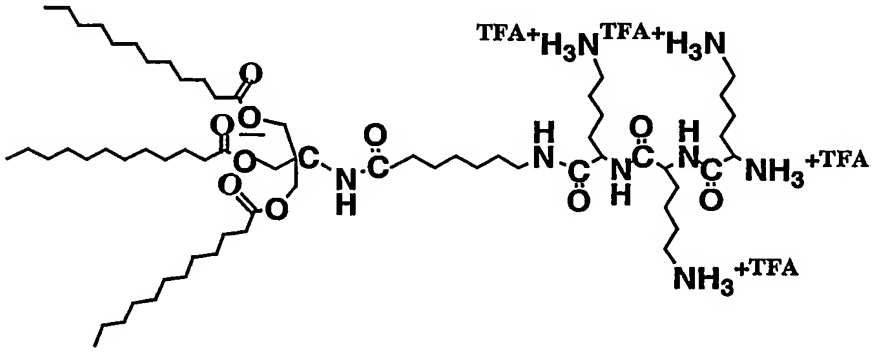
11. A method as claimed in claim 10 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.

12. A method as claimed in any one of claims 1 to 11 in which the lipid is a cationic lipid.

13. A method as claimed in any one of claims 1 to 12 in which the lipid is CSO87 having the formula :



14. A method as claimed in any one of claims 1 to 12 which the lipid is CSO60 having the formula:



15. A method as claimed in any one of claims 1 to 6 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.

16. A composition comprising

(i) an engineered ovine atadenovirus; and

(ii) a lipid,

wherein the engineered ovine atadenovirus comprises a promoter and a gene encoding an enzyme which converts a prodrug to a cytotoxic metabolite, the gene being under the control of the promoter.

17. A composition as claimed in claim 16 in which the promoter is selectively active in a specific tissue.

18. A composition as claimed in claim 16 or claim 17 in which the promoter is a prostate specific membrane antigen promoter.

19. A composition as claimed in any one of claims 16 to 18 in which the promoter is a probasin promoter.

20. A composition as claimed in any one of claims 16 to 19 in which the ovine atadenovirus further comprises a transcriptional enhancer element.

21. A composition as claimed in claim 20 in which the transcriptional enhancer element is from the prostate specific membrane antigen gene.

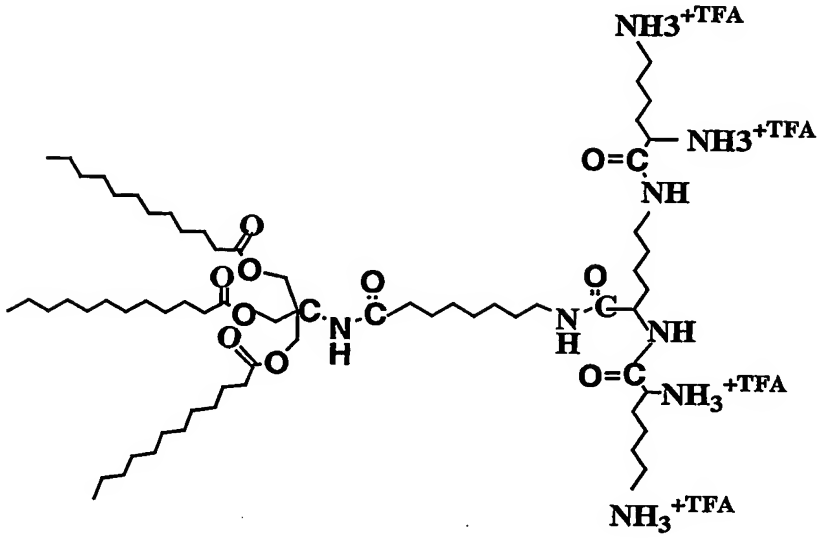
22. A composition as claimed in any one of claims 16 to 21 in which the enzyme and the prodrug are an enzyme/prodrug combination selected from the group consisting of thymidine kinase/ganciclovir, thymidine kinase/acyclovir, bacterial cytosine deaminase /5-flurocytosine, human cytochrome P450/cyclophosphamide or ifosfamide, thymidine phosphorylase/5'-deoxy-5-flurouridine, cytosine kinase/cytosine arabinoside, *E. coli* GPT/ 6-thioxanthine, *E. coli* nitroreductase/5(-aziridine-1-yl)-2,4-dinitrobenzamide, and bacterial purine nucleoside phosphorylase/6-methylpurine-2-deoxyriboside or fludarabine.

23. A composition as claimed in any one of claims 16 to 21 in which the enzyme is a purine nucleoside phosphorylase (PNP) and the prodrug is a purine prodrug which is converted by PNP to a toxic purine metabolite.

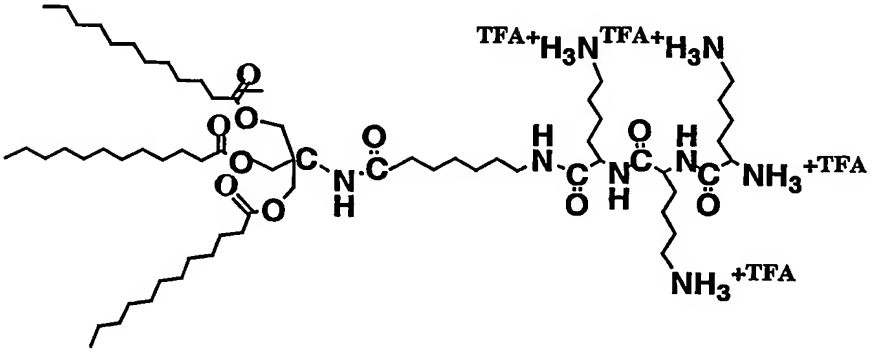
24. A composition as claimed in claim 23 in which the prodrug is 6-methyl purine-2-deoxyriboside (6MPDR) or fludarabine.

25. A composition as claimed in any one of claims 16 to 24 in which the lipid is a cationic lipid.

26. A composition as claimed in any one of claims 16 to 25 in which the lipid is CSO87 having the formula :



27. A composition as claimed in any one of claims [illegible] which the lipid is CSO60 having the formula:



28. A composition as claimed in any one of claims 16 to 27 in which the engineered ovine atadenovirus is selected from the group consisting of OAdV220, OAdV223 and OAdV623.